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L1: Entry 6 of 10 File: USPT Oct 5, 1999

DOCUMENT-IDENTIFIER: US 5962318 A
TITLE: Cytotoxic T lymphocyte-mediated immunotherapy

BSPR:
In such a situation, one may wish to isolate and expand the CTL clone(s) that specifically recognizes the subdominant antigen of choice, e.g., LMP-2a, or one may wish to develop methods for culturing CTLs in vitro that only recognize LMP-2a, i.e., they are monospecific. In order to maximize the T cell response to a weak immunogen, the target antigen would need to be expressed on the surface of a powerful antigen presenting cell. Thus, there is a need in the art to develop a system that provides for high level presentation of the weak antigen on an effective antigen presenting cell. There is a further need to generate antigen specific CTLs to induce both primary and memory T cell responses to a subdominant antigen. There is still a further specific need to develop a transduction system that provides for high level expression of a foreign gene in antigen presenting cells, and application of such a system to generate CTLs for the treatment of malignancies expressing specific viral or tumor antigens.

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L2: Entry 19 of 30 File: USPT Oct 27, 1998

DOCUMENT-IDENTIFIER: US 5827642 A
TITLE: Rapid expansion method ("REM") for in vitro propagation of T lymphocytes

ABPL:
The present invention provides a rapid expansion method (termed "REM"), for quickly generating large numbers of T lymphocytes, including cytolytic and helper T lymphocytes. REM involves culturing the T cells in association with a disproportionately large concentration of nondividing feeder cells, preferably .gamma.-irradiated peripheral blood mononuclear cells ("PBMC") present at an excess of at least 40-fold (relative to the number of target T cells), more preferably at an excess of at least about 200-fold. Cultures grown under REM exhibit dramatically enhanced expansion rates that can be even further elevated by the use of appropriate concentrations of an additional feeder cell, an anti-CD3 monoclonal antibody and IL-2, as described herein. Clonal expansions in the range of 500-fold to 3000-fold can be achieved within a single stimulation cycle of about 10-13 days, which is more than 100-fold more efficient than currently employed methods of culturing human T cell clones. Genetic transduction efficiencies were also enhanced using REM-expanded T lymphocytes. Several examples involving human bone marrow transplant recipients illustrate the effective use of REM-expanded antigen-specific cytotoxic T lymphocytes for adoptive immunotherapy in humans.

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L3: Entry 1 of 8 File: USPT Aug 21, 2001

DOCUMENT-IDENTIFIER: US 6277368 B1
TITLE: Cancer immunotherapy using autologous tumor cells combined with cells expressing a membrane cytokine

ORPL:
Kruse et al., "Analysis of interleukin 2 and various effector cell populations in adoptive immunotherapy of 9L rat gliosarcoma: Allogeneic cytotoxic T lymphocytes prevent tumor take" Proc. Natl. Acad. Sci. USA (1990) 87:9577-9581.